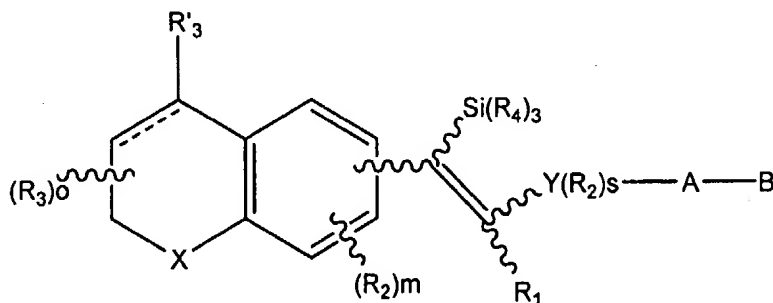


Amendments to the Claims

Please cancel Claims 8-11 and 32-40. Please amend Claims 1, 2, 5, 12, and 13. Please add new Claims 41-60. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1. (Currently amended) A method of treating an FXR-mediated pathological condition selected from hypercholesterolemia and hyperlipoproteinemia in a mammal comprising the step of administering to a mammal in need thereof a pharmaceutically acceptable composition comprising a synthetic FXR ligand able to stimulate, block or inhibit the activity of a mammalian FXR receptor, said synthetic FXR ligand comprising a compound of the formula a compound of the formula:



formula (3)

wherein the dashed line represents a bond or absence of a bond;

X is S , O , NR' where R' is H or alkyl of 1 to 6 carbons, or X is $(C(R_1)_2)_n$ where R_1 is H or alkyl of 1 to 6 carbons, and n is an integer having the value of 0 to 1;

R_2 is hydrogen, lower alkyl of 1 to 6 carbons, F, Cl, Br, I, CF_3 , fluoro substituted alkyl of 1 to 6 carbons, OH, SH, alkoxy of 1 to 12 carbons, or alkylthio of 1 to 12 carbons, benzyloxy or C_1 - C_{12} alkylbenzyloxy;

R_3 is hydrogen, lower alkyl of 1 to 6 carbons or F;

m is an integer having the value of 0-3;

o is an integer having the value of 0-4 when the dashed line represents absence of a bond, and 0-3 when the dashed line represents a bond;

R'_3 is hydrogen, lower alkyl of 1 to 6 carbons, F or $(R_{15})_r$ -phenyl, $(R_{15})_r$ -naphthyl, or $(R_{15})_r$ -heteroaryl where the heteroaryl group has 1 to 3 heteroatoms selected from the group consisting of O, S and H, r is an integer having the values of 0-5;

R_4 is alkyl of 1 to 8 carbons, or phenyl;

s is an integer having the value of 0-2;

Y is phenyl or naphthyl group, or heteroaryl selected from a group consisting of pyridyl, thienyl, furyl, pyridazinyl, pyrimidinyl, pyrazinyl, thiazolyl, oxazolyl, imidazolyl and pyrazolyl, said phenyl and heteroaryl groups being optionally substituted with one or two R_2 groups;

R_{15} is independently H, F, Cl, Br, I, NO_2 , $N(R_8)_2$, $NH(R_8)$, COR_8 , $NR_8CON(R_8)_2$, OH, $OCOR_8$, OR_8 , CN, an alkyl group having 1 to 10 carbons, fluoro substituted alkyl group having 1 to 10 carbons, an alkenyl group having 1 to 10 carbons and 1 to 3 double bonds, alkynyl group having 1 to 10 carbons and 1 to 3 triple bonds, or a trialkylsilyl or trialkylsilyloxy group where the alkyl groups independently have 1 to 6 carbons;

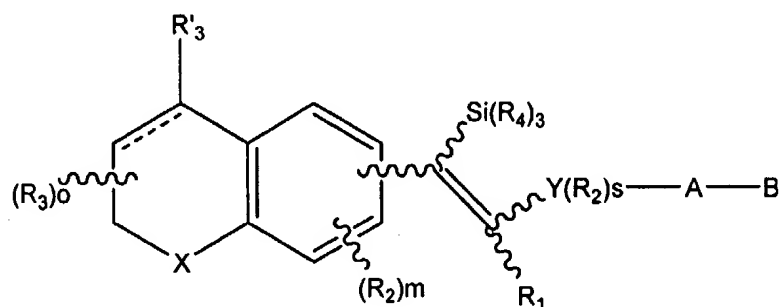
A is $(CH_2)_q$ where q is 0-5, lower branched chain alkyl having 3-6 carbons cycloalkyl having 3-6 carbons, alkenyl having 2-6 carbons and 1 or 2 double bonds, alkynyl having 2-6 carbons and 1 or 2 triple bonds;

B is hydrogen, $COOH$, NO_2 , $P(O)(OH)_2$, $P(O)(OH)OR_8$, $P(O)(OR_8)_2$, SO_2OH , $SO_2(OR_8)$, $COOR_8$, $CONR_9R_{10}$, $-CH_2OH$, CH_2OR_{11} , CH_2OCOR_{11} , CHO , $CH(OR_{12})_2$, $CHOR_{13}O$, $-COR_7$, $CR_7(OR_{12})_2$, $CR_7OR_{13}O$, or tri-lower alkylsilyl, where R_7 is an alkyl, cycloalkyl or alkenyl group containing 1 to 5 carbons, R_8 is an alkyl group of 1 to 10 carbons or trimethylsilylalkyl where the alkyl group has 1 to 10 carbons, or a cycloalkyl group of 5 to 10 carbons, or R_8 is phenyl or lower alkylphenyl, R_9 and R_{10} independently are hydrogen, an alkyl group of 1 to 10 carbons, or a cycloalkyl group of 5-10 carbons, or phenyl or lower alkylphenyl, R_{11} is lower alkyl, phenyl or lower alkylphenyl, R_{12} is lower alkyl, and R_{13} is divalent alkyl radical of 2-5 carbons, or a pharmaceutically acceptable salt of said compound.

2. (Currently amended) A method in accordance with Claim 1 where X is ~~$(C(R_1)_2)_n$~~ $(C(R_{1,2}))_n$ and n is 1.
3. (Original) A method in accordance with Claim 1 where X is S.
4. (Original) A method in accordance with Claim 1 where X is O.
5. (Currently amended) A method in accordance with Claim 1 where X is ~~NR~~ NR'.
6. (Original) A method in accordance with Claim 1 where Y is phenyl.
7. (Original) A method in accordance with Claim 1 where Y is thienyl.
- 8-11. (Canceled)

12. (Currently amended) A method in accordance with Claim ~~11~~ 1 wherein said compound has a structure of formula (3) where the dashed line represents a bond.
13. (Currently amended) A method in accordance with Claim ~~11~~ 1 wherein said compound has a structure of formula (3) where the dashed line represents a bond.
- 14-30 (Canceled)

31. (Previously presented) A method of treating a hypercholesterolemic mammal comprising the steps: administering to a mammal in need thereof a pharmaceutically acceptable composition comprising an FXR antagonist having the following formula



formula (3)

wherein the dashed line represents a bond or absence of a bond;

X is S , O , NR' where R' is H or alkyl of 1 to 6 carbons, or X is $(C(R_1)_2)_n$ where R_1 is H or alkyl of 1 to 6 carbons, and n is an integer having the value of 0 to 1;

R_2 is hydrogen, lower alkyl of 1 to 6 carbons, F, Cl, Br, I, CF_3 , fluoro substituted alkyl of 1 to 6 carbons, OH, SH, alkoxy of 1 to 12 carbons, or alkylthio of 1 to 12 carbons, benzyloxy or C_1 - C_{12} alkylbenzyloxy;

R_3 is hydrogen, lower alkyl of 1 to 6 carbons or F;

m is an integer having the value of 0-3;

o is an integer having the value of 0-4 when the dashed line represents absence of a bond, and 0-3 when the dashed line represents a bond;

R'_3 is hydrogen, lower alkyl of 1 to 6 carbons, F or $(R_{15})_r$ -phenyl, $(R_{15})_r$ -naphthyl, or $(R_{15})_r$ -heteroaryl where the heteroaryl group has 1 to 3 heteroatoms selected from the group consisting of O, S and H, r is an integer having the values of 0-5;

R_4 is alkyl of 1 to 8 carbons, or phenyl;

Y is phenyl or naphthyl group, or heteroaryl selected from a group consisting of pyridyl, thienyl, furyl, pyridazinyl, pyrimidinyl, pyrazinyl, thiazolyl, oxazolyl, imidazolyl and pyrrazolyl, said phenyl and heteroaryl groups being optionally substituted with one or two R_2 groups;

s is an integer having the value of 0-2;

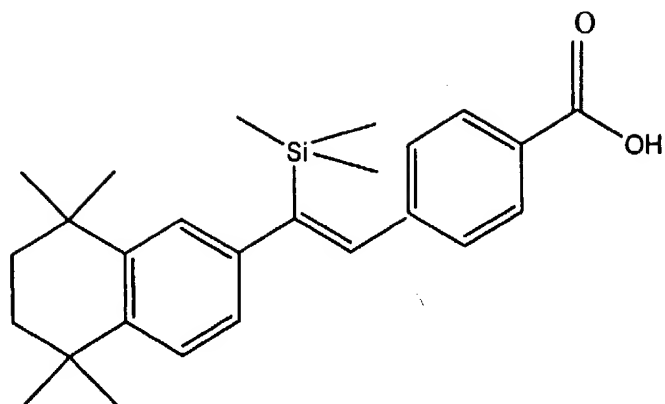
R_{15} is independently H, F, Cl, Br, I, NO_2 , $N(R_8)_2$, $NH(R_8)$, COR_8 , $NR_8CON(R_8)_2$, OH, $OCOR_8$, OR_8 , CN, an alkyl group having 1 to 10 carbons, fluoro substituted alkyl group having 1 to 10 carbons, an alkenyl group having 1 to 10 carbons and 1 to 3 double bonds, alkynyl group having 1 to 10 carbons and 1 to 3 triple bonds, or a trialkylsilyl or trialkylsilyloxy group where the alkyl groups independently have 1 to 6 carbons;

A is $(CH_2)_q$ where q is 0-5, lower branched chain alkyl having 3-6 carbons cycloalkyl having 3-6 carbons, alkenyl having 2-6 carbons and 1 or 2 double bonds, alkynyl having 2-6 carbons and 1 or 2 triple bonds;

B is hydrogen, $COOH$, NO_2 , $P(O)(OH)_2$, $P(O)(OH)OR_8$, $P(O)(OR_8)_2$, SO_2OH , $SO_2(OR_8)$, $COOR_8$, $CONR_9R_{10}$, $-CH_2OH$, CH_2OR_{11} , CH_2OCOR_{11} , CHO , $CH(OR_{12})_2$, $CHOR_{13}O$, $-COR_7$, $CR_7(OR_{12})_2$, $CR_7OR_{13}O$, or tri-lower alkylsilyl, where R_7 is an alkyl, cycloalkyl or alkenyl group containing 1 to 5 carbons, R_8 is an alkyl group of 1 to 10 carbons or trimethylsilylalkyl where the alkyl group has 1 to 10 carbons, or a cycloalkyl group of 5 to 10 carbons, or R_8 is phenyl or lower alkylphenyl, R_9 and R_{10} independently are hydrogen, an alkyl group of 1 to 10 carbons, or a cycloalkyl group of 5-10 carbons, or phenyl or lower alkylphenyl, R_{11} is lower alkyl, phenyl or lower alkylphenyl, R_{12} is lower alkyl, and R_{13} is divalent alkyl radical of 2-5 carbons, or a pharmaceutically acceptable salt of said compound.

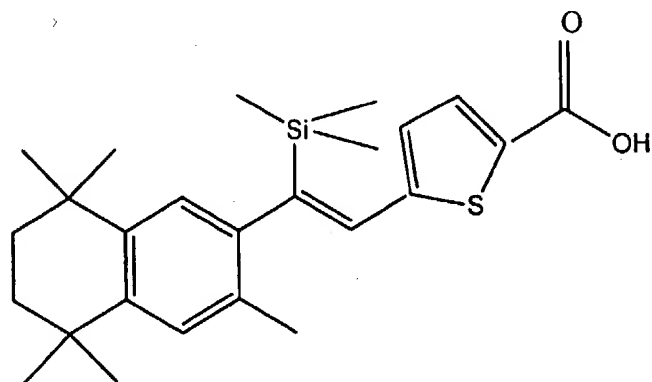
32-40 (Canceled)

41. (New) A method in accordance with Claim 1 where R_2 is H and R_4 is ethyl.
42. (New) A method in accordance with Claim 41 where B is CH_2OH .
43. (New) A method in accordance with Claim 41 where B is $COOR_8$.
44. (New) A method in accordance with Claim 1 where the compound of formula(3) is



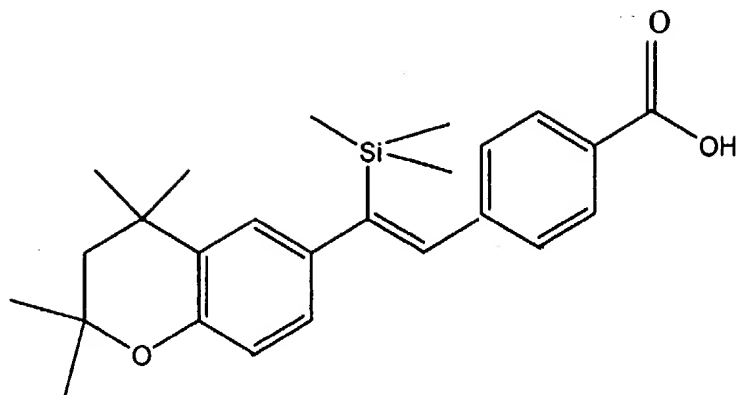
or a pharmaceutically acceptable salt thereof.

45. (New) The method in accordance with Claim 1 where the compound of formula (3) is



or a pharmaceutically acceptable salt thereof.

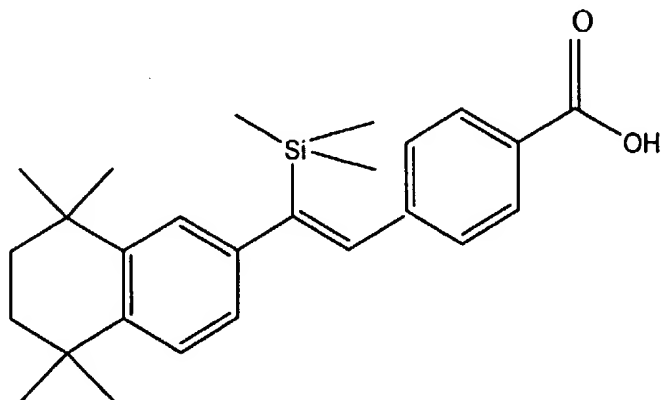
46. (New) The method in accordance with claim 1 where the compound of formula (3) is



or a pharmaceutically acceptable salt thereof.

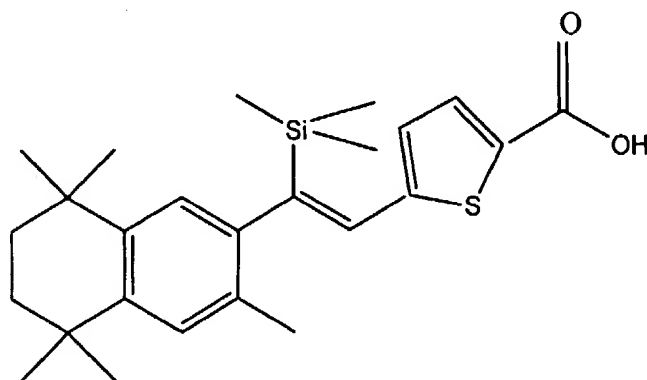
47. (New) A method in accordance with Claim 31 where R_2 is H and R_4 is ethyl.
48. (New) A method in accordance with Claim 47 where B is CH_2OH .
49. (New) A method in accordance with Claim 47 where B is $COOR_8$.
50. (New) A method in accordance with Claim 31 where X is $(C(R_1)_2)_n$ and n is 1.
51. (New) A method in accordance with Claim 31 where X is S.
52. (New) A method in accordance with Claim 31 where X is O.
53. (New) A method in accordance with Claim 31 where X is NR' .
54. (New) A method in accordance with Claim 31 where Y is phenyl.

55. (New) A method in accordance with Claim 31 where Y is thienyl.
56. (New) A method in accordance with Claim 31 where the compound of formula(3) is



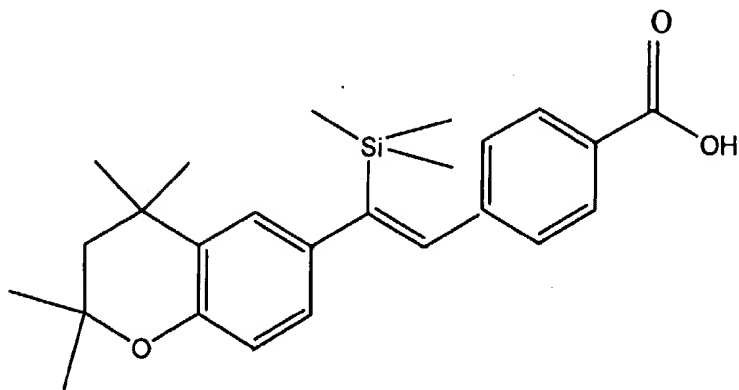
or a pharmaceutically acceptable salt thereof.

57. (New) The method in accordance with Claim 31 where the compound of formula (3) is



or a pharmaceutically acceptable salt thereof.

58. (New) The method in accordance with Claim 31 where the compound of formula (3) is



or a pharmaceutically acceptable salt thereof.

59. (New) A method of treating an FXR-mediated pathological condition selected from hypercholesterolemia and hyperlipoproteinemia in a mammal comprising the step of administering to a mammal in need thereof a pharmaceutically acceptable composition comprising (Z)-5-[2-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)-2-(trimethylsilyl)vinyl]thiophene-2-carboxylic acid.
60. (New) A method of treating a hypercholesterolemic mammal comprising the steps: administering to a mammal in need thereof a pharmaceutically acceptable composition comprising an FXR antagonist (Z)-5-[2-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)-2-(trimethylsilyl)vinyl]thiophene-2-carboxylic acid.